REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the amendments above and comments below.

Claims 9-29 are pending in the present application. Claims 10-12 and 19-29 have been withdrawn from consideration. Accordingly, claims 9 and 13-18 are presented for examination on the merits.

Claim 9 has been amended to place the claim in a different, and provide sequence identification. The claim, as well as claims 14-18, has been amended to clarify that the claimed enzyme is a recombinant enzyme, as disclosed throughout the specification. The claim has also been amended to recite that the claimed recombinant enzyme has at least about 75% sequence identity with SEQ ID NO. 8. Sequence identification numbers have also been inserted in claims 14-18 where appropriate. Claim 16 has been amended to recite that the DNA molecule hybridizes under high stringency conditions, which is disclosed and defined at page 4, first paragraph and page 15, second paragraph. No new matter is added by these amendments to the claims.

I. Rejection of Claims 9 and 13-17 Under 35 U.S.C § 112, Second Paragraph

Claims 9 and 13-17 stand rejected under 35 U.S.C § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the use of abbreviations and failure to provide a SEQ ID NO. for the polypeptides recited in the claims renders these claims indefinite.

It is respectfully submitted that the amendments to the claims render this formal ground of rejection moot.

II. Rejection of Claim 16 Under 35 U.S.C § 112, Second Paragraph

Claim 16 is rejected under 35 U.S.C § 112, second paragraph. The Examiner states that the term "hybridizes thereto is indefinite.

It is respectfully submitted that the amendment to claim 16 renders this ground of rejection moot.

III. Rejection of Claim 18 Under 35 U.S.C § 112, Second Paragraph

Claim 16 is rejected under 35 U.S.C § 112, second paragraph. the Examiner states that the lack of sequence identifiers and use of abbreviations render the claim indefinite.

It is respectfully submitted that the amendments to claim 18 render this ground of rejection moot.

IV. Rejection of Claims 9, and 13-18 Under 35 U.S.C § 112, First Paragraph

Claims 9 and 13-18 stand rejected under 35 U.S.C § 112, first paragraph. the Examiner states that the specification is enabling for enzymes having SEQ ID NO. 1, 3 aaor 5 and having a single specified substitution at position 251 and capable of hydrolyzing organophosphates. The Examiner asserts, however, that the specification does not enable any such enzymes encoded by polynucleotides having at least 60% homology to the polynucleotides encoding the above-referenced enzymes. In particular,

the Examiner states that the specification does not establish regions of the protein that may be modified or a rational and predictable scheme for modifying the amino acid residues while retaining activity.

Applicants respectfully disagree with the Examiner's assertions.

The present invention is directed to recombinant enzymes having organophosphate degrading activity. Applicants have isolated and characterized three independent malathion resistant clones of the *Lucilia cuprina* gene encoding protein E3. Applicants have also isolated and characterized the orthologous gene from the housefly, *Musca domestica* as described on pages 13-16 of the specification. As shown in the specification, the *M. domestica* E3 polypeptide shares 75% sequence identity with the L. cuprina polypeptide. *See* Figure 2 for sequence alignment of the *M. domestica and L. cuprina* LcαE7 .

The present claims are directed to recombinant enzymes having a specified activity, having a Leu, Ala, Ser, ILe, Val, Thr, Cys, Met or Gly residue at position 251 and which have at least about 75% sequence identity with SEQ ID NO. 8. The specification shows through sequence alignments that the protein conferring malathion resistance can tolerate up to at least 25% sequence variation. The sequence alignments also demonstrate that it is essential for malation resistance that the tryptophan at position 251 is replaced with a less bulky amino acid, i.e., Leu, Ser, Ala, Ile, Val, Thr, Met or Gly. Thus, the specification clearly demonstrates to one of skill in the art that numerous amino acid substitutions may be made while retaining the claimed enzyme activity. One of skill in the art at the time of the invention could readily introduce amino acid changes into the sequence based on the data provided in the specification, and expect to obtain functional

enzymes having the claimed specificity, without undue experimentation. In particular, one of skill in the art at the time was capable of utilizing the disclosed alignment data to make conservative amino acid substitutions in the claimed recombinant enzyme.

Furthermore, the claimed recombinant enzyme is readily obtainable by performing nucleic acid hybridization with a probe having a sequence of any of the disclosed allele sequences under appropriate hybridization conditions, and expressing the protein and testing for activity as taught in the specification. One of skill in the art is capable of obtaining polynucleotide sequences encoding the claimed poylpeptide. Indeed, claims to such polynucleotides encoding the enzyme have issued in US 6,235,515 (the parent application).

The specification teaches how to obtain the DNA encoding the claimed polypeptides, and teaches how to test for the claimed activity. The specification also provides several examples of recombinant enzymes as claimed, obtained from different species. Using the methods set forth in the specification, Applicants obtained several recombinant polypeptides having the claimed activity from different species and exhibiting up to 25 % amino acid variation.

Accordingly, the rejection of claims 9 and 13-18 under 35 U.S.C § 112, first paragraph is respectfully traversed.

V. Rejection of Claims 9 and 13-18 Under 35 U.S.C § 102(b)

Claims 9 and 13-18 stand rejected under 35 U.S.C § 102(b) over Whyard et al., Pesticide Biochemistry and Physiology (Whyard I) or Whyard et al., Biochemical

Genetics (Whyard II). The Examiner states that the cited prior art discloses a naturally occurring (non-recombinant protein) having the claimed sequence and activity.

This rejection is respectfully traversed as follows.

The claimed invention is directed to a recombinant enzyme having organophosphate hydrolyzing activity and having at least about 75% sequence identity with SEQ ID NO. 8, except that the tryptophan at position 251 is substituted with a less bulky amino acid selected from a specified group of amino acids.

In contrast, the cited prior art references disclose isolation and purification of a naturally occurring *L. cuprina* polypeptide having malathion resistance. Neither of the cited references discloses the amino acid sequence of the *L. cuprina* polypeptide, or the nucleotide sequence of the gene encoding the polypeptide. Thus, neither cited prior art reference anticipates the claimed recombinant enzyme.

Furthermore, these prior art references do not render the claimed recombinant enzyme obvious. Neither reference provides sequence information concerning the *L. cuprina* enzyme or any structurally related malathion resistant enzyme. Without such sequence information, one of ordinary skill in the art would not have found it obvious to generate recombinant enzymes, particularly recombinant enzymes having at least about 75% sequence identity with SEQ ID NO. 8.

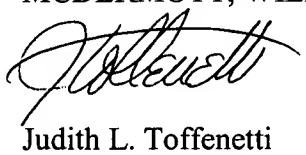
Accordingly, the rejection of claims 8 and 13-18 under 35 U.S.C § 102(b) over Whyard I or Whyard II is respectfully traversed.

It is respectfully submitted that the present application, as amended above, is in condition for allowance, an early notification thereof being earnestly solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT, WILL & EMERY



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